Crystal Structure and Absolute Configuration of Bromoisotenulin

By **Mazhar-Ul-Haque,** Chemistry Department, Pahlavi University, Shiraz, Iran
**Donald Rogers,*** Chemical Crystallography Laboratory, Imperial College, London SW7 2AY
Charles N. Caughlan, Department of Chemistry, Montana State University, Bozeman, Montana 59715, U.S.A.

Bromoisotenulin crystallises in the monoclinic space group $P2_1$, $a = 8 \cdot 732(3)$, $b = 23 \cdot 094(6)$, $c = 10 \cdot 237(5)$ Å, $\beta = 121 \cdot 27(10)°$, $Z = 4$, with two independent molecules in the asymmetric unit. Two sets of data were collected : photographic, 2300 reflections, and diffractometer, 1700 reflections. The structure was solved by Patterson and heavy-atom methods, and the diffractometer data refined by full-matrix least-squares to R 0·075. The results confirm the structure (IV) suggested by Herz *et al.* and supply the unknown stereochemistry and absolute configuration. The carbon skeleton is biogenetically abnormal, a methyl group having migrated from C(4) to C(5). Both five-membered rings are *trans*-fused to the seven-membered ring. Attention is drawn to an error in the published stereochemistry of the related compound, bromomexicanin E.

THE sesquiterpene bitter principle tenulin, $C_{17}H_{22}O_5$, was isolated by Clark[1] from several *Helenium* species. Its properties were studied,[2-4] and although much chemical work was done on this and similar compounds, little progress was made towards elucidating their structures. Barton and de Mayo[5] suggested formulae (I) and (II) for tenulin and isotenulin. Later, Braun *et al.*[6] repeated much of this work, but indicated a different position for the carbonyl group in the unsaturated five-membered ring. In order to resolve this difference and to determine the detailed stereochemistry we undertook an X-ray diffraction study of crystals of the derivative,

bromoisotenulin, first described by Clark.[7] After the present work was started, however, some n.m.r. studies of

(I)   (II)

(III)
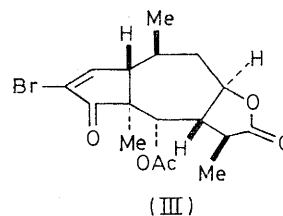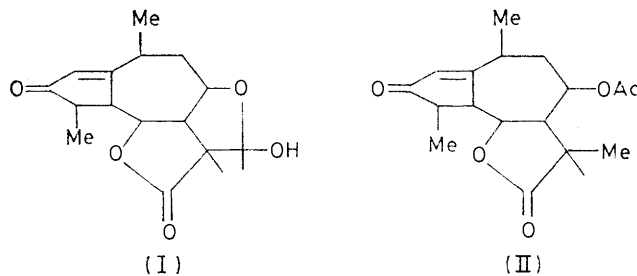
Herz *et al.*[8] threw doubt on the correctness of both formulae (I) and (II), and later work[9] led them to

[1] E. P. Clark, *J. Amer. Chem. Soc.*, 1939, **61**, 1836.
[2] E. P. Clark, *J. Amer. Chem. Soc.*, 1940, **62**, pp. 597, 2154.
[3] H. E. Ungnade and E. C. Hendley, *J. Amer. Chem. Soc.*, 1948, **70**, 3921.
[4] H. E. Ungnade, E. C. Hendley, and W. Dunkel, *J. Amer. Chem. Soc.*, 1950, **72**, 3818.
[5] D. H. R. Barton and P. de Mayo, *J. Chem. Soc.*, 1956, 142.
[6] B. H. Braun, W. Herz, and K. Rabindran, *J. Amer. Chem. Soc.*, 1956, **75**, 4423.
[7] E. P. Clark, *J. Amer. Chem. Soc.*, 1939, **61**, 1840.
[8] W. Herz, H. Watanabe, M. Miyazaki, and Y. Kishida, *J. Amer. Chem. Soc.*, 1962, **84**, 2601.
[9] W. Herz, W. A. Rohde, K. Rabindran, P. Jayaraman, and N. Viswanathan, *J. Amer. Chem. Soc.*, 1962, **84**, 3857.

suggest a revised skeletal structure. Our results confirmed the revision and supplied the missing relative stereochemistry, which in a preliminary publication [10]

(IV)
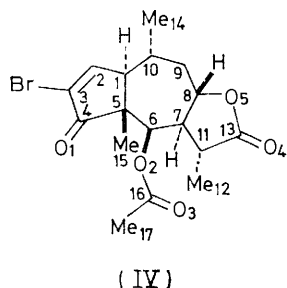
we had represented as (III). But, as later work by Herz *et al.*[11] using o.r.d. measurements had suggested that bromoisotenulin has the opposite chirality, we checked it by Bijvoet's anomalous dispersion method and found it should indeed be reversed to (IV).

EXPERIMENTAL

Crystals were faintly yellow plates.

Crystal Data.—$C_{17}H_{21}BrO_5$, $M = 385\cdot24$. Monoclinic, $a = 8\cdot732(3)$, $b = 23\cdot094(6)$, $c = 10\cdot237(5)$ Å, $\beta = 121\cdot27(10)°$, $U = 1764\cdot5$ Å^3, $D_m = 1\cdot451(2)$, $Z = 4$, $D_c = 1\cdot450$ g cm^{-3}, $F(000) = 792$. Optical activity and systematic absences indicate space group $P2_1$, so the asymmetric unit comprises two independent molecules. μ (Cu-K_α) $= 31\cdot1$ cm^{-1}; λ (Cu-K_α) $= 1\cdot54178$ Å.

In view of the relatively high absorption, attempts were made to grind spheres but were unsuccessful. Instead, we used a block, *ca.* 0·4 mm square, cut from a plate *ca.* 0·33 mm thick. For lack of an absorption program at the time this work was done, no absorption correction was applied.

The structure was solved and refined from photographic data measured visually from multiple-film Weissenberg photographs of the layers 0—7kl and hk0. *Ca.* 2300 independent reflections were recorded, corrected for Lorentz and polarisation factors, and correlated *via* the hk0 reflections. Estimates of the scale and temperature factors were obtained from a Wilson plot for the 0kl data. The preliminary work [10] (Imperial College) was based entirely on the photographic data.

Four years later, while one of us (M. U. H.) was working at Bozeman, a fresh set of intensity data was obtained from the same crystal by use of a diffractometer. This was with a view to improving the accuracy of the structure and getting reliable data for the Bijvoet anomalous dispersion technique.[12] During the four-year interval (and later) the crystal developed a slow progressive staining which was noticeably accelerated by exposure to X-radiation. This partial decomposition may have contributed to the lower number of reflections measurable on the diffractometer, which was a manually operated General Electric XRD 5 fitted with a scintillation counter and used with Cu-K_α radiation. Reflections were recorded by a θ—2θ (moving

crystal–moving counter) method using a 100 s scan (2° min^{-1} for 2θ) and 50 s for background on each side of the peak. Of 2500 reflections scanned, only 1700 had a net intensity $> 1\sigma(I)$. The intensities were corrected for Lorentz and polarisation factors,[13] but not for absorption.

Solution and Refinement of the Structure.—The three-dimensional Patterson revealed two independent pairs of bromine positions with quite different y co-ordinates, which in space group $P2_1$ was a convenience in several ways. First, a higher than usual proportion (*ca.* 2000) of the 2300 photographic reflections were successfully phased by the bromine atoms; secondly, they destroyed the pseudo-mirror plane found in the initial Fourier maps for $P2_1$ when phased by only one set of heavy atoms; and thirdly, the ability to compare two independent molecules has at all stages been a great help and gratifying compensation for the extra effort needed to refine the molecules.

All the 44 carbon and oxygen atoms were fairly quickly identified among the 50 strongest peaks in the bromine-phased Fourier map, and they were refined by use of Rollett's least-squares program. The bromine atoms were refined anisotropically and the oxygen and carbon atoms isotropically from R 0·35 to 0·12. The occurrence of some rather large discrepancies in bond lengths was one reason for remeasuring the intensities.

The atomic parameters from the photographic data were used as the starting point for refinement of the diffractometer data. Three cycles of ORFLS [14] full-matrix least-squares refinement of co-ordinates and isotropic thermal parameters reduced R to 0·14. Eight more cycles were carried out in which all non-hydrogen atoms were refined anisotropically and allowance was made for 18 non-methyl hydrogens in calculated (non-refined) positions, each of which was given an isotropic B factor 0·5 Å^2 greater than the equivalent isotropic value for its parent carbon atom. Unit weights were used at this stage and refinement was discontinued when the average shift to error ratio was *ca.* 0·1 for all atoms except those in the acetate group. R based on the 1700 terms was 0·075.

Later, as a matter of interest, the limit on observable reflections was lowered to 0·5$\sigma(I)$. This brought in an extra 277 terms, all of which were among the terms measured visually. Inclusion of these terms and the introduction of statistical weights [15] gave a slight rise in R to 0·0772, but appreciably lower standard derivations for co-ordinates. (A change in computing facilities and the increased size of the job dictated that this last stage was refined by block-diagonal least-squares only: Ahmed's program [13] was used.)

Two attempts were made to determine the absolute configuration. In the first, Bijvoet anomalies [12] were measured visually from the photographs for 30 sensitive reflections. 24 Indicated that our published configuration (III) was wrong. Later, corrections $\Delta f'$ and $\Delta f''$ for bromine atoms and Cu-K_α radiation (taken from ref. 16) were applied to

[10] D. Rogers and Mazhar-Ul-Haque, *Proc. Chem. Soc.*, 1963, 92, and Mazhar-Ul-Haque, Ph.D. Thesis, University of London, 1964.

[11] W. Herz, A. Romo de Vivar, J. Romo, and N. Viswanathan, *Tetrahedron*, 1963. **19**, 1350.

[12] A. F. Peerdeman, A. J. van Bommel, and J. M. Bijvoet, *Proc., k. ned. Akad. Wetenschap*, 1951, **54**, 3; see also *Nature*, 1951, **68**, 271.

[13] NRC2, Data reduction program, by F. R. Ahmed and C. P. Saunderson; NRC10, Block-diagonal least-squares program, by F. R. Ahmed, National Research Council, Ottowa; both these programs were adapted for the SDS Sigma 7, and others were written by G. D. Smith, C. N. Caughlan, and E. L. Enwall.

[14] W. R. Busing, K. O. Martin, and H. A. Levy, ORFLS program, Oak Ridge, National Laboratory, Oak Ridge, Tennessee, 1962.

[15] G. H. Stout and L. H. Jensen, ' X-Ray Structure Determination,' Macmillan, New York, 1968, 457.

[16] ' International Tables of X-Ray Crystallography,' vol. III, Kynoch Press, Birmingham, 1968, 214.

TABLE 1

Fractional co-ordinates for the non-hydrogen atoms ($\times 10^4$), with standard deviations in parentheses

Atom	Molecule (1) x	y	z	Molecule (2) x	y	z
Br	−327(3)	3542(1)	7040(4)	3521(4)	5000(0)	7887(3)
C(1)	1149(20)	1800(6)	7191(19)	4344(22)	3684(5)	5476(18)
C(2)	898(24)	2374(7)	7904(21)	4306(26)	3932(7)	6748(20)
C(3)	60(24)	2742(7)	6719(20)	3692(28)	4482(8)	6470(23)
C(4)	−527(18)	2541(6)	5278(16)	3061(22)	4648(7)	4960(17)
C(5)	−198(13)	1859(5)	5457(15)	2999(16)	4082(6)	4094(14)
C(6)	608(15)	1656(5)	4521(15)	3600(17)	4225(6)	2977(13)
C(7)	1817(16)	1094(5)	5163(14)	4566(18)	3681(6)	2728(18)
C(8)	989(20)	658(5)	5790(18)	3679(18)	3100(6)	2608(16)
C(9)	1681(31)	701(8)	7468(20)	4356(19)	2776(5)	4058(15)
C(10)	1054(26)	1224(7)	8022(22)	3886(20)	3012(5)	5193(17)
C(11)	2110(22)	780(6)	4007(19)	4577(21)	3718(6)	1267(17)
C(12)	3660(30)	953(8)	3887(29)	6300(25)	4065(9)	1501(27)
C(13)	2202(22)	165(6)	4578(19)	4574(24)	3099(7)	866(18)
C(14)	2174(34)	1272(8)	9759(17)	5008(34)	2681(7)	6767(21)
C(15)	−2064(26)	1619(8)	4951(23)	919(23)	3895(7)	3296(21)
C(16)	−926(28)	1790(7)	1791(22)	1969(32)	4905(10)	889(23)
C(17)	−2589(31)	1669(11)	286(23)	8(66)	4924(15)	−478(30)
O(1)	−1074(20)	2803(5)	4091(19)	2542(16)	5125(4)	4383(13)
O(2)	−873(14)	1551(4)	2997(12)	2014(15)	4343(5)	1592(12)
O(3)	275(21)	2063(8)	1873(19)	3353(32)	5207(7)	1524(24)
O(4)	2750(19)	−267(5)	4161(17)	5018(21)	2911(7)	−19(17)
O(5)	1725(17)	94(4)	5603(14)	4139(15)	2753(4)	1640(15)

all the diffractometer data [$>0\cdot5\sigma(I)$] for both structures (III) and (IV). They gave R 0·0794 for (III) and 0·0772 for (IV), a difference in favour of (IV) which has a significance level $\gg$0·99 (Hamilton [17]).

DESCRIPTION AND DISCUSSION OF THE STRUCTURE

The numbering scheme used is depicted in (IV). Final atomic positions for structure (IV), referred to right-handed axes, are listed with their standard deviations in Table 1, and the calculated co-ordinates of the

TABLE 2

Calculated positional co-ordinates ($\times 10^4$) for hydrogen atoms (excluding those in methyl groups)

	Molecule (1) x	y	z	Molecule (2) x	y	z
H(1)—C(1)	2339	1811	7277	5589	3735	5669
H(2)—C(2)	1300	2449	9029	4732	3728	7760
H(3)—C(6)	1391	1981	4516	4499	4557	3432
H(4)—C(7)	3066	1204	6023	5846	3653	3625
H(5)—C(8)	−339	741	5239	2363	3178	2185
H(6)—C(9)	3072	741	8009	5703	2769	4579
H(7)—C(9)	1444	334	7831	3899	2369	3792
H(8)—C(10)	−253	1149	7694	2565	2958	4768
H(9)—C(11)	1084	838	2938	3501	3927	−473

non-methyl hydrogens are given in Table 2. Interatomic distances, valence angles, and torsion angles are listed in Tables 3—5 respectively, and the intermolecular contacts (<3·6 Å) in Table 6. Observed and calculated structure factors are tabulated in Supplementary Publication No. SUP 20880 (2 pp., 1 microfiche),* together with the anisotropic thermal parameters of the atoms in Table 1.

Figure 1 shows the [100] projection of the structure and confirms the stereochemical and chiral identity of

* See Notice to Authors No. 7 in *J.C.S. Dalton*, 1972, index issue.

[17] W. C. Hamilton, *Acta Cryst.*, 1965, **18**, 502.

TABLE 3

Bond lengths (Å), with standard deviations in parentheses

	Molecule (1)	Molecule (2)
Br—C(3)	1·94(2)	1·95(2)
C(1)—C(2)	1·58(2)	1·44(3) *
C(1)—C(5)	1·54(2)	1·58(2)
C(1)—C(10)	1·60(2)	1·59(2)
C(2)—C(3)	1·34(2)	1·35(3)
C(3)—C(4)	1·37(2)	1·40(3)
C(4)—C(5)	1·60(2)	1·57(2)
C(4)—O(1)	1·21(2)	1·22(2)
C(5)—C(6)	1·53(2)	1·52(2)
C(5)—C(15)	1·53(3)	1·62(3) *
C(6)—C(7)	1·58(2)	1·61(2)
C(6)—O(2)	1·44(2)	1·40(2)
C(7)—C(8)	1·56(2)	1·52(2)
C(7)—C(11)	1·52(2)	1·50(2)
C(8)—C(9)	1·50(2)	1·48(2)
C(8)—O(5)	1·51(2)	1·48(2)
C(9)—C(10)	1·55(3)	1·52(2)
C(10)—C(14)	1·53(2)	1·58(2)
C(11)—C(12)	1·48(4)	1·61(3) *
C(11)—C(13)	1·52(2)	1·49(2)
C(13)—O(4)	1·27(2)	1·23(2)
C(13)—O(5)	1·33(2)	1·31(2)
C(16)—C(17)	1·50(3)	1·55(5)
C(16)—O(2)	1·33(2)	1·48(3) *
C(16)—O(3)	1·19(3)	1·25(4)

* Discrepancy between the two molecules *ca.* >3σ.

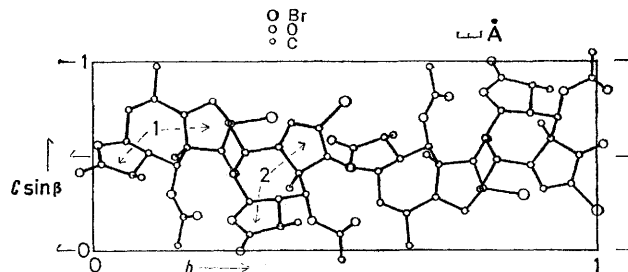

FIGURE 1 The [100] projection of the structure of (IV) showing the two independent molcules

the two independent molecules. Figure 2 (a and b) shows stereopairs for each molecule. The conformational details and even the torsion angles match very closely.

TABLE 4

Valence angles (deg.), with standard deviations in parentheses

	Molecule (1)	Molecule (2)
C(2)–C(1)–C(5)	104·5(13)	102·8(14)
C(2)–C(1)–C(10)	113·1(14)	115·6(15)
C(5)–C(1)–C(10)	117·7(14)	113·9(13)
C(1)–C(2)–C(3)	104·7(16)	112·2(18)
Br–C(3)–C(2)	120·7(15)	126·6(17)
Br–C(3)–C(4)	120·4(14)	121·1(15)
C(2)–C(3)–C(4)	118·9(17)	112·2(19)
C(3)–C(4)–C(5)	105·5(13)	105·9(15)
C(3)–C(4)–O(1)	130·1(17)	128·2(18)
C(5)–C(4)–O(1)	124·2(14)	125·8(16)
C(1)–C(5)–C(4)	101·8(11)	100·9(12)
C(1)–C(5)–C(6)	111·7(11)	114·4(12)
C(1)–C(5)–C(15)	113·5(13)	114·5(12)
C(4)–C(5)–C(6)	110·2(11)	108·7(12)
C(4)–C(5)–C(15)	102·9(12)	102·1(12)
C(6)–C(5)–C(15)	115·6(12)	114·4(12)
C(5)–C(6)–C(7)	114·6(11)	111·4(11)
C(5)–C(6)–O(2)	106·5(11)	104·9(11)
C(7)–C(6)–O(2)	110·0(11)	108·5(12)
C(6)–C(7)–C(8)	110·4(11)	114·6(12)
C(6)–C(7)–C(11)	114·4(12)	112·8(13)
C(8)–C(7)–C(11)	108·2(12)	103·6(13)
C(7)–C(8)–C(9)	115·5(14)	116·2(13)
C(7)–C(8)–O(5)	100·8(14)	103·2(12)
C(9)–C(8)–O(5)	105·0(14)	106·9(12)
C(8)–C(9)–C(10)	117·6(17)	117·3(13)
C(1)–C(10)–C(9)	109·0(16)	110·3(13)
C(1)–C(10)–C(14)	112·3(16)	108·7(14)
C(9)–C(10)–C(14)	110·5(17)	109·7(14)
C(7)–C(11)–C(12)	117·9(16)	111·7(14)
C(7)–C(11)–C(13)	98·2(13)	102·6(13)
C(12)–C(11)–C(13)	114·6(16)	112·8(15)
C(11)–C(13)–O(4)	123·8(16)	125·7(17)
C(11)–C(13)–O(5)	116·4(15)	112·3(15)
O(4)–C(13)–O(5)	119·8(16)	121·9(17)
C(17)–C(16)–O(2)	115·2(18)	101·7(22)
C(17)–C(16)–O(3)	121·5(21)	140·6(27)
O(2)–C(16)–O(3)	123·3(20)	117·7(22)
C(6)–O(2)–C(16)	121·0(13)	115·3(14)
C(8)–O(5)–C(13)	108·9(13)	109·7(13)

Mean bond lengths (Å) derived from the diffractometer data for the two molecules are much as expected:

	No. of bonds	Molecule (1)	Molecule (2)
$C(sp^3)$–$C(sp^3)$	11	1·54 Å	1·56 Å
$C(sp^3)$–$C(sp^2)$	4	1·55	1·51
C–O	4	1·40	1·42
$C(sp^2)=O$	3	1·22	1·23

But there are four rather large discrepancies between corresponding bonds (Table 3), each >3σ. We do not regard them as being chemically significant, however, partly because there are no abnormalities in the molecular packing or conformations that would require such aberrations, and partly because the standard deviations (0·02—0·05 Å and 1·1—2·7°) which were calculated from the block-diagonal least-squares matrix should, to be realistic, be increased by ca. 50—60%. The resulting fairly high standard deviations and individual large discrepancies are probably attributable to the paucity of the diffractometer data and the absence of an absorption correction. The highest standard deviations occur in the acetate groups [especially for molecule (2)] and are

TABLE 5

(a) Torsion angles around the ring perimeters. Each angle is printed opposite the second atom in the string of four which define the angle.

	Molecule (1)	Molecule (2)
C(16)	−176·9	−173·8
O(2)	127·7	126·2
C(6)	−86·0	−93·4
C(5)	−136·1	−141·3
C(4)	6·8	10·1
C(3)	7·1	6·7
C(2)	−147·4	−144·7
C(1)	−168·9	−167·9
C(10)	−44·0	−49·9
C(9)	−176·3	−174·0
C(8)	−141·0	−143·4
O(5)	6·7	3·4
C(13)	10·8	15·1
C(11)	−147·0	−150·8

(b) Some torsion angles (deg.) involving peripheral atoms.

	Molecule (1)	Molecule (2)
C(2)–C(3)–C(4)–O(1)	−168·4	−174·4
C(3)–C(4)–C(5)–C(15)	100·1	97·5
C(5)–C(4)–C(3)–Br	−172·8	−166·7
C(6)–C(5)–C(4)–O(1)	39·4	43·1
C(6)–O(2)–C(16)–O(3)	5·9	4·0
C(6)–C(7)–C(11)–C(12)	89·5	88·1
O(4)–C(13)–C(11)–C(12)	−41·2	−40·6
O(5)–C(13)–C(11)–C(12)	136·7	135·4
C(8)–O(5)–C(13)–O(4)	−175·3	179·7
C(7)–C(11)–C(13)–O(4)	−167·1	−161·0
C(8)–C(9)–C(10)–C(14)	−167·9	−160·6
C(2)–C(1)–C(10)–C(14)	−46·2	−47·7
C(6)–C(7)–C(8)–C(9)	−93·8	−91·5
C(11)–C(7)–C(8)–O(5)	27·8	28·5
C(10)–C(1)–C(5)–C(6)	−95·1	−94·1
C(2)–C(1)–C(5)–C(4)	20·9	23·7
C(5)–C(6)–C(7)–C(8)	38·4	40·8
C(7)–C(8)–C(9)–C(10)	73·7	71·5
C(5)–C(1)–C(10)–C(9)	68·9	73·3
C(1)–C(5)–C(6)–C(7)	39·8	37·8
C(4)–C(5)–C(6)–O(2)	−86·0	−93·4
C(15)–C(5)–C(6)–O(2)	30·0	20·0
C(11)–C(7)–C(6)–O(2)	40·9	44·1

TABLE 6

Intermolecular contacts (Å) <3·6 Å

Atoms *		Atoms *	
Br · · · O(4ᴵ)	3·30	O(1) · · · O(5′ᴵᴵᴵ)	3·59
C(2) · · · O(4′ᴵᴵ)	3·33	O(4) · · · C(1′ᴵⱽ)	3·39
C(2) · · · C(13′ᴵᴵ)	3·49	O(4) · · · C(3′ᴵⱽ)	3·53
C(2) · · · O(5′ᴵᴵ)	3·49	O(4) · · · C(4′ᴵⱽ)	3·29
C(8) · · · O(1′ᴵ)	3·24	O(4) · · · C(5′ᴵⱽ)	3·51
C(9) · · · O(1′ᴵ)	3·42	O(4) · · · C(6′ᴵⱽ)	3·23
C(12) · · · O(1′ᴵ)	3·42	O(4) · · · C(17′ᴵⱽ)	3·28
C(15) · · · O(1′ᴵ)	3·58	O(5) · · · C(12′ᴵⱽ)	3·48
C(17) · · · O(4′ᴵᴵᴵ)	3·47	C(12) · · · C(15′ⱽ)	3·48
O(1) · · · C(13′ᴵᴵᴵ)	3·58		

Roman numeral superscripts refer to the following equivalent positions:

I $-x, \frac{1}{2} + y, -z$	IV $-x, y - \frac{1}{2}, z$
II $x, y, 1 + z$	V $1 + x, y, z$
III x, y, z	

* Primed atoms are in molecule (2), unprimed in molecule (1).

doubtless associated with the generally higher thermal parameters prevailing in these groups.

Comparison of these results with those derived from the photographic data reveals several large discrepancies, e.g. the Br–C(3) bonds are 0·06 and 0·10 Å longer, using the diffractometer data, and some valence angles differ by as much as 9°. Apart from the relatively larger

random errors in the visually estimated data [as shown by the calculated standard deviations (*ca.* 0·03 Å and *ca.* 3·6° for these particular quantities) and the usual underestimation of such values] it is likely that appreciable systematic errors are responsible for these discrepancies. Thus both sets of data had absorption errors which were different but had not been allowed for

membered ring. In the unsaturated carbocyclic ring the four atoms defined by the double bond are virtually coplanar (dihedral angles only 7·1 and 6·7°) and atom C(5) deviates strongly to the β-side of the plane. In the lactone ring, atoms C(11), C(13), O(5), and C(18) are nearly coplanar (dihedral angles 6·7 and 3·4°) and atom C(7) deviates to the α-side. The bonds across which the
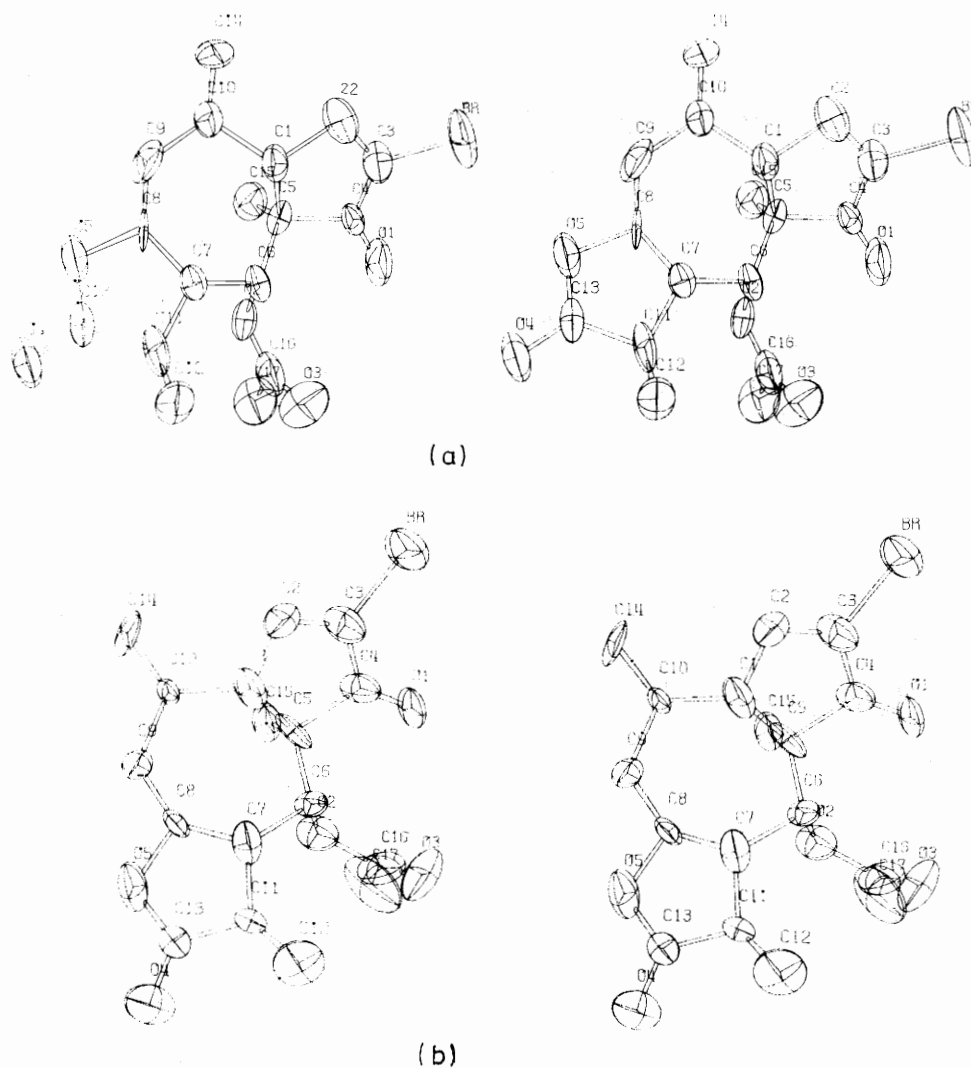
FIGURE 2 Stereopairs for molecules (1) and (2) in the structure of (IV)

in either case, and no allowance had been made with the photographic data for either anomalous dispersion or for a weighting scheme. This is a salutary reminder of the danger of a naïve appeal to calculated standard deviations alone.

The carbon skeleton of bromoisotenulin is biogenetically abnormal since a methyl group has migrated from position 4 to 5. On dehydrogenation it is not eliminated, but migrates back to 4 to give chamazulene.[5] The lactone ring and acetyl group are interchanged as compared with Barton and de Mayo's structure (II). Both five-membered rings are *trans*-fused to the seven-

rings are fused are quite steeply skewed. The whole ring system, though strongly puckered is relatively flat, and all three rings (but especially the seven-membered ring) if shorn of their substituents approximate closely to a two-fold axis of symmetry through C(6) and the mid point of C(9)–C(10).

There are no specially short intermolecular distances (Table 6) and nothing but Van der Waals' contacts, so that, apart from the acetyl groups whose orientations do differ slightly due to different environments, the molecules are not under significant constraints and hence correspond closely in their conformational details.

It is interesting to compare this with related compounds from *Helenium* species, *i.e.* bromohelenalin [18] (V)

(V)   (VI)
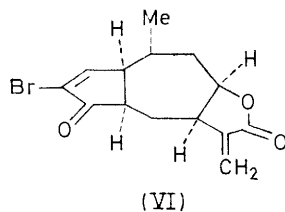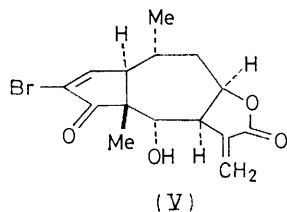
and bromomexicanin E (VI).[19] * In (V) the five-membered carbocyclic ring is *trans*-fused to the seven-membered ring, while the lactone is *cis*-fused. In (VI) both five-membered rings are *cis*-fused to the seven-membered ring, the fusions being *cis-syn-cis*. All three compounds are appreciably folded.

The structure and relative stereochemistry of bromo-isotenulin played a key role in determining the stereochemistry of four *Helenium* constituents, dihydroiso-tenulin, tetrahydrohelenalin, dihydromexicanin E, and

tetrahydrobalduilin. Herz *et al.*[11] showed from a variety of chemical and n.m.r. evidence that the configurations at C(1) and C(10) are the same in all these compounds, and they were able to construct a table of the relative configurations at C(5)—(8), and C(11). From the X-ray results for bromoisotenulin they were then able to assign the full absolute stereochemistry to each of the congeners. The results seem to be consistent with all the observed chemistry throughout the group.

* The stereochemistry of the methyl group at C(10) in (VI) was inadvertently drawn β in ref. 19. It should have been α, as shown here.

[18] M. T. Emerson, C. N. Caughlan, and W. Herz, *Tetrahedron Letters*, 1964, **12**, 821; and Mazhar-Ul-Haque, and C. N. Caughlan, *J. Chem. Soc.* (*B*), 1969, 956.
[19] Mazhar-Ul-Haque and C. N. Caughlan, *J. Chem. Soc.* (*B*), 1967, 355.